UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,001,890 B1
DATED : February 21, 2006
INVENTOR(S) : Hermann Wagner et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 12,
Line 43, insert the following:

Table 2 Sequences of oligomers and death due to lethal shock

a		
1668	TCCATGACGTTCCTGATGCT	(SEQ ID NO: 4)
CRE	ATTGCCTGACGTCAGAGAGC	(SEQ ID NO: 5)
1668-CA	TCCATGACGTCACTGATGCT	(SEQ ID NO: 6)
CRE-TC	*ATTGCCT*GACGTTC*GAGAGC*	(SEQ ID NO: 7)
b		
1668	5/5	
CRE	0/5	
1668-CA	0/3	
CRE-TC	3/3	

Lethality was determined as in Example 2. The 1668 sequence fortuitously contains a combination of transcription response elements, namely the transcription factor binding sites (TGACGTTCC). This element represents the binding site for HSVIP04 (ATF), HSINS04 (CREB half site), CAMV35SR03 (HBP-1a yeast) or ADE422 (AP-1) in combination with an HSIL606 site which is a repressor site (sequence analysis from EMBL database Heidelberg). This sequence can be found in the 5' non-coding regions (promoters) of several eukaryotic cytokine genes including human IL-13 promoter and IL-12 p40 intron 1. The CRE sequence contains all the response elements cited above except for HSIL606 and it contains the full CRE palindromic sequence (TGACGTCA). In accordance with the invention, the CRE sequence did not induce death and changes in the 1668 eliminate toxicity.

TNF-α release is a hallmark of lethal toxic shock [Tracey, K. J. et al., Science 234, 470-474 (1986), Tracey, K. J. et al., Nature 330, 662-664 (1987)]. An exchange of only two nucleotides between CRE and 1668 resulted in a loss of macrophage induced TNF-α release activity. The sequence of the corresponding oligonucleotide is given in Table 2. The reported 6-mer active core sequence of 1668 contains the CpG flanked by two 5' purines and two 3' pyrimidines. The exchange of CA for TC does not affect this motif, however, TNF-α release was severely diminished. Thus, the broader core 8-mer sequence or the transcription response element and not the surrounding sequence environment was responsible for these effects. In accordance with the invention, when utilizing macrophage derived TNF-α release as a marker, the information comprised in the prior art 5'Pu-Pu-CpG-Py-Py-3' motif alone was not satisfactory for predicting oligomer activity or toxicity. Additionally, in contrast to 1668, CRE did not induce IL-6 release in vivo or from the ANA-1 cell line in vitro.

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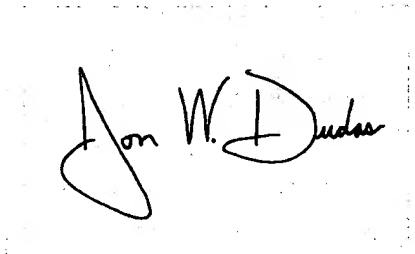
Column 13,
Line 49, the title of Table 4, "Sequence of ukary tic TRE te t d" should read -- Sequences of eukaryotic TRE tested --.
Line 58, Table 4, "STAT 4 CTGATTTCCCCGAAATGATG (SEQ ID NO: 19)" should read -- STAT 4 CTGATTTCCCCGAAATGATG (SEQ ID NO: 19) --.

Signed and Sealed this

Thirtieth Day of May, 2006



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